REMARKS

Reconsideration of the subject application is requested in view of the above amendments and the following remarks.

I. Claim Status. Claims 1, 7, and 17 have been amended. Claims 5, 6 and 20-35 are canceled without prejudice or disclaimer.

Claim 1 has been amended to replace the phrase "about 6 to about 45" with "about 6 to 45". No new matter is added by this amendment.

Claim 7 has been amended to properly depend from claim 1, following cancellation of claim 6 in a prior Amendment. The scope of claim 7 is unchanged.

Claim 17 has been rewritten from a dependent claim to an independent claim, incorporating the elements of the claims from which it previously depended. The scope of claim 17 is unchanged.

By this Amendment, no new matter has been introduced into the application.

Upon entry of this Amendment, claims 1-4 and 7-19 are pending. No new claims have been added to the application. The amendments to claims 1, 7 and 17 do not raise additional issues that need to be searched by the Examiner. Accordingly, the present Amendment should be entered.

II. Claim Rejections. The claim rejections set forth in the Final Office Action are summarized and addressed as follows:

(i) Rejections Under 35 U.S.C. §112, first paragraph (enablement). Claims 1-4 and 7-19 remain rejected as allegedly failing to be enabled by the specification. The amended claims call for a peptide epitope sequence of about 6 to 45 amino acids in length. The Examiner asserts

that the specification fails to enable one of ordinary skill in the art to make and use the invention when the peptide epitope called for in the claims is less than 10 amino acids in length.

The Examiner's position is that, "The state of the Art [sic] casts doubt on the use of scaffolding for IgG production from allergens and there is evidence in Applicant's specification that an 8-mer did not induce a protective IgG response." The Examiner's position is not well taken.

With respect to the prior art, the Examiner has cited King et al., Ref. 3 on IDS submitted on 10-15-03, (Int. Arch. Allergy Immunol., 2001, 124:85-86) ("King") for the proposition that "hybrid proteins with 20-30 amino acid residues in the peptide epitope sequence have maximal reduction in allergenicity while still retaining adequate immunogenicity." *See* Office Action dated February 1, 2005 ("Feb. 1 Office Action") at page 3. On its face, however, there is nothing in this statement that suggests that a peptide epitope of 6-10 amino acids would fail to elicit a protective IgG response. There is no requirement that the claimed embodiments of the invention be restricted to "maximal" activity. Moreover, the claims call for the epitope to be present in a surface accessible region of the hybrid protein corresponding to its position in the allergen protein. The surface accessibility further promotes immunogenicity of the peptide epitope.

Additionally, at the time the instant application was filed, it was well known among those of ordinary skill in the art peptide epitopes of six amino acids are effective in eliciting an antibody response. For example, in the context of discussing production of anti-peptide antibodies, Harlow et al., "Antibodies: A Laboratory Manual," 1988, Cold Spring Harbor Laboratories, pp. 72-78 ("Harlow") states that, "The smallest synthetic peptides that will consistently elicit antibodies that bind to the original protein are 6 residues in length." Harlow at page 76, section entitled "Size of Peptide." Hence, by the filing date of the instant application, the general understanding that peptides of 6 amino acids can "consistently" elicit an immune response was so well established that

the statement appeared in a practical, "how-to" manual for immunologists. The Examiner has failed to provide any evidence in the prior art suggesting that although it is well accepted that 6 amino acid epitopes are effective immunogens generally, they would not be effective immunogens when present in the claimed hybrid allergens.

In the only other reference cited in connection with the instant rejection, the Examiner cites Patent Application publication US 2004/0171116 A1 ("the '116 Publication") for the proposition that insertion of peptides fragments will destabilize the three-dimensional structure of a protein. The examples of hybrid allergens bearing peptide epitopes and which retain a native conformation that are set forth in the specification, however, disprove this proposition. Moreover, the Examiner acknowledges that the specification is enabling for hybrid allergens bearing peptide epitopes of at least ten amino acids in length. The '116 Publication includes no information that would lead one of ordinary skill in the art to conclude that peptide epitopes of 6 amino acids would be more likely to destabilize the three-dimensional structure of a protein than would a 10 amino acid epitope. It is counterintuitive to assert that an epitope of shorter length would have greater effect to destabilize a scaffold protein, especially when the short peptide is derived from a solvent exposed region, as called for in the claims. Thus, any general teaching in the '116 Publication that peptide epitopes destabilize proteins is refuted by the instant specification.

The Examiner also relies on '116 Publication for the proposition that linear epitopes are not suitable for grafting three dimensional epitopes from allergens to scaffolding proteins. In response, Applicants first decline to characterize the peptide epitopes called for in the claims as linear or conformational. The peptide epitopes are grafted into a homologous position of a homologous allergen and may or may not represent a linear epitope, a conformational epitope or some combination of linear and conformational epitopes. Applicants need not specify the

mechanism by which the claimed invention works to obtain a patent. In any event, the specification, includes one example of a 9 amino acid epitope (EA-PV 142-150), one example of a 10 amino acid epitope (EA-PV 195-204) and two examples of 11 amino acid epitopes (EA-PV 22-32 and EA-PV 115-125). Each of these epitopes were inserted into a scaffold protein and used to illicit an IgG response. The '116 Publication includes no information suggesting that a 6 amino acid epitope would be any less immunogenic than epitopes of between 9-11 amino acids in length. This is especially so in light of the prior art's recognition that peptides of 6 amino acids "consistently" elicit an antibody response. Harlow, *supra*. Thus any general teaching in the '116 Publication relating to the immunogenicity of linear epitopes does not raise any doubts that the specification enables claims calling for a peptide epitope of at least 6 amino.

In summary, neither King nor the '116 Publication includes any information that would lead one of ordinary skill in the art to conclude that the specification fails to enable peptide epitopes of 6 amino acids, rather than 10 amino acids. Thus, the Examiner's position that the specification fails to enable claims calling for a peptide epitope of at least 6 amino acids is reduced to an alleged failure of a particular 8 amino acid epitope to elicit an IgG response. It is well established, however, that a claim may include inoperative embodiments. That one particular 8 amino acid epitope may fail to elicit an IgG response must be balanced against the success of obtaining an IgG response with 4 different epitopes that are between 9-11 amino acids in length.

The Examiner, in essence, has imposed a requirement that each embodiment claim 1 be exemplified by a working example. This is not the standard for enablement. The presence or absence of a working example is only one consideration for enablement. An examination of all the Wands factors shows that the full scope of the instant claims is enabled. The specification includes numerous examples showing that the nature of invention (an allergen hybrid protein comprising a

peptide epitope in a homologous scaffolding) is generally enabled. The state of the art is such that epitopes of 6 amino acids are considered generally immunogenic. The state of the art provides no legitimate reason to suspect that epitopes of 6-9 amino acids would destabilize a protein when it is shown by examples that epitopes of 10 amino acids do not. The level of one of ordinary skill in the art is high. The inventors provide guidance on how to make the hybrid allergens, use them as immunogens, and tests for an IgG response. It is predictable in the art that when used for immunizations, a native protein will illicit an IgG response, to a greater or lesser extent, to epitopes spread across the surface of the protein; and the instant specification reports that at least 4 out 4 other epitopes of 9-11 amino acids successfully produced an IgG response. Finally, the breadth of the claim sought (a peptide epitope of at least 6 amino acids) is close to the scope of the claim for which the specification provides four working examples (9-11 amino acids). Hence, the great weight of the Wands factors falls in favor of enablement of the full breadth of the present.

For all of the reasons set forth above, the specification enables one of ordinary skill in the art to make and use the full scope of the claimed invention. Withdrawal of the rejection of claims 1-4 and 7-19 for lack of enablement is requested, accordingly.

(ii) Rejections Under 35 U.S.C. §102. Claims 1-4 and 10-17 remain rejected as allegedly anticipated by Monsalve et al., *Allergy Clin. Immunol.* 103(1) Part 2:S181, 1999 ("Monsalve I") or Monsalve et al., *Arb. Paul Ehrlich Inst.* 93:181-188, 1999 ("Monsalve II"), as evidenced by King et al., *Intl. Arch. Allergy Immunol.* 124:85-86, 2001 ("King et al."). The Examiner alleges that the art teaches a peptide epitope according to claim 1 of 49 amino acids, upon which the phrase "about 45" reads. In response, without conceding the validity of the rejection, claim 1 has been amended to replace the phrase "about 6 to about 45" with "about 6 to 45". This

clearly indicates that the peptide epitope of claim 1 does not read upon epitopes of 49 amino acids. The present rejection should therefore be withdrawn.

(iii) Rejections Under 35 U.S.C. §103. Claims 1 and 18 remain rejected as allegedly obvious over either Monsalve I or Monsalve II, as evidenced by King et al., in view of Alibhai et al., U.S. Patent No. 6,639,054 ("Alibhai et al."). The Examiner continues to allege that there is motivation to combine the teachings of Alibhai et al. with those of Monsalve I and II and King et al. In response, without conceding the validity of the rejection, claim 1 has been amended, as above.

The amended claims are not obvious over the prior art of record. A *prima facie* case for obviousness under 35 U.S.C. § 103(a) can only be established by showing all of the elements of the invention are disclosed, that there was a concrete suggestion or motivation to modify or combine the teachings of the prior art, coupled with a reasonable expectation of success (M.P.E.P § 2142). The motivation and the reasonable expectation of success must be found in the prior art and not in the Applicants' disclosure. *See* M.P.E.P. § 2142, citing *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

The art cited does not recite or suggest, when taken alone or in combination, all of the elements of claim 1. As presented above, Monsalve I and II and King et al. do not teach, or suggest, a hybrid allergen comprising a peptide epitope of about 6 to 45 amino acids within a scaffold protein and wherein the epitope sequence is present in a surface accessible region of the hybrid protein corresponding to its position in the allergen protein. None of the hybrid proteins of Monsalve I and Monsalve II include peptide epitopes that are 6-45 amino acids in length. Nor does the prior art of record include any suggestion or incentive to make hybrid allergens bearing smaller peptide epitopes (*i.e.*, about 6 to 45 amino acids). Additionally, the prior art or record fails to

suggest that a grafted epitope sequence should be present in a surface accessible region of a hybrid protein corresponding to its position in the allergen protein, as called for in the claims.

The teachings of Alibhai et al. do not remedy the deficiencies of Monsalve I and II and King et al. Alibhai et al. fails to provide any incentive to shorten the epitopes used in the hybrid proteins of Monsalve I and II below 49 amino acids. For at least this reason, amended claims 1 and 18 are not obvious over the prior art of record. Withdrawal of this rejection is requested.

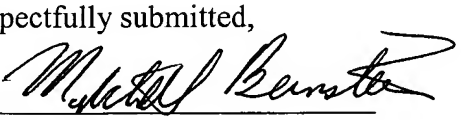
CONCLUSION

In view of the above remarks, it is respectfully requested that the application be reconsidered and that all pending claims be allowed and the case passed to issue.

If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Dated: December 21, 2005

Respectfully submitted,

By 

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